ON THE NATURE OF THE NERVE IMPULSE

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The nerve fiber, as is well known, shows not only the highest degree of irritability, but also possesses power to transmit a state of excitation in the most efficient manner. Our interest in the study of the nerve impulse lies not only in the fact that the nervous system is one of the most important factors in all organic activities in the higher animals, but also, in the fact that it constitutes the center of a general problem that deals with the mechanism by which a living substance adjusts itself to its environment.

In order to study the nature of the nerve impulse, many physiologists have investigated what takes place in the nerve fiber during the conduction of the impulse. The results were very peculiar: there were no structural changes of any kind, no heat production, and there appeared to be no production of carbon dioxide, nor did they find any change in the distribution of the organic materials in the tissue. When electrical changes were discovered in the stimulated nerve, the problem was considered to be settled once for all. The idea that the nerve impulse is of an electrical nature was, however, soon doubted, when Helmholtz observed that the velocity of the nerve impulse is of an entirely different magnitude from that of an electrical current. One thing seemed to be certain: that the nerve impulse can pass through the fiber without consuming any material. The fact that we can not detect fatigability in the nerve after continuous stimulation supported the belief that certain quickly reversible physical conditions exist in the nerve, and that changes in these conditions must determine the phenomena of excitability and conductivity in the nerve. Such changes were thought to be either of the colloidal state, of the surface tension, or of the permeability of the nerve.

With the new apparatus which measures as little carbon dioxide as one ten-millionth gram, we have demonstrated that an isolated nerve fiber gives off a definite amount of carbon dioxide and that when it is stimulated this carbon dioxide production is more than doubled. These facts not only indicate that there is another kind of functional change beside the electrical, but also show that the chemical changes in the nerve fiber are of the same magnitude as those of other organs.

To some physiologists, however, our results do not seem to be con-

clusive enough to show that the carbon dioxide given off by an isolated nerve is produced by life processes. Experimental conditions, to their minds, might have caused the tissue to decompose in a manner quite different from its normal behavior.

Further experiments show the following facts:

1. If the sciatic nerve is removed from a frog, it shows an electrical response for many hours. Since electrical changes are characteristic only of living nerves, we consider that the isolated nerve does not die for many hours. If measurements are made on an isolated nerve at successive time intervals, we find that carbon dioxide production steadily decreases as the nerve approaches death The point of minimum carbon dioxide production corresponds nearly to the point where electrical response ceases. The dead nerve gives almost no carbon dioxide.

2. Although the nerve remains active for some time without oxygen, it is a known fact that absence of oxygen diminishes the excitability of the nerve. The carbon dioxide production of a nerve fiber is much less in hydrogen than in atmospheric air. We should expect that there would be no difference under these two conditions if the carbon dioxide production of an isolated nerve fiber were due entirely to the death process.

3. The normal, uncut fiber in the body is very susceptible to many chemical reagents. A weak concentration of an anesthetic, for instance, renders the nerve nore excitable, or stimulates it, while a higher concentration makes it unexcitable. These reagents show similar effects on the carbon dioxide production of the cut nerve.

These facts, to my mind, indicate that the production of carbon dioxide from an isolated nerve fiber is at least a correct expression of what is going on in the normal nerve in the body, and indicate clearly that the normal nerve must have a chemical activity which is accelerated when the nerve is stimulated.

If the chemical activity is so vigorous as our results indicate, one naturally asks how we can explain the fact that the nerve impulse can pass continuously for hours without any measurable sign of fatigue. Apparent lack of fatigability in the nerve is a remarkable fact, but I wonder whether we should be willing to ignore the presence of metabolic activity in the contracting wings of insects which can fly continuously for hours at a rate of as high as three hundred vibrations per second. The ordinary induction coil we use for fatigue experiments, by the way, maintains not more than one hundred vibrations per second, at the maximum.

Granting that the absence of fatigability in the nerve, as measured by ordinary methods, may not be a question of absence of metabolism, but merely of the speed at which breaking and repairing processes of the tissue come to equilibrium, one may still ask how we explain the lack of heat production. Snyder reported very recently[1] that a smooth muscle failed to show any sign of heat formation during contraction, which, no one doubts, increases carbon dioxide production. When we dip a zinc rod into copper sulphate solution we observe heat formation, but that with proper arrangements, as in a Daniell cell, the reaction goes on practically isothermally, all the chemical energy being converted into electrical energy. I do not think that we should ignore the increase of carbon dioxide production in the nerve on stimulation because of the fact that we cannot detect heat formation.

There are some physiologists who admit that the living nerve should be chemically active to maintain a 'normal' condition, like any other living tissue, but who hold that the increase in carbon dioxide production on stimulation must be a secondary effect due to primary physical changes. We will consider this question in a quite different way.

The state of a nerve fiber depends upon three conditions: the degree of irritability, the direction of the impulse and the rate of the impulse. The relation of these conditions to chemical activity in the nerve is analyzed in the following way:

1. Degree of irritability and carbon dioxide production.

We have already cited the fact that chemical reagents which modify the degree of excitability invariably modify the rate of carbon dioxide production in the same proportion. The chemical activity in the nerve fiber seems to determine the state of nerve excitability.

2. The direction of nerve impulse and carbon dioxide production.

If one takes nerve bundles containing only sensory fibers, which conduct the normal nerve impulse in a central direction, the portion of the nerve nearer the natural source of the nerve impulse (i.e., nearer the end organ) gives more carbon dioxide than the portion away from it. There is a gradient of carbon dioxide production in the unstimulated nerve. This gradient of chemical condition seems to determine the direction of nerve impulse. Many experiments made on various kinds of pure nerve fibers enable us to generalize this by saying that the normal nerve impulse passes toward a point of lower carbon dioxide production.

3. Rate of the nerve impulse and carbon dioxide production.

There seems to exist a close relation between the rate of nerve impulse and carbon dioxide production in the resting nerve, if one com-

pares the corresponding nerves of different animals. The data for such a generalization must necessarily be cumulative. The limited data we have secured indicate that the nerves which give off more carbon dioxide in the resting state conduct the nerve impulse more quickly.*

I may add here that conditions which influence the speed of the nerve impulse modify the chemical activity of the resting nerve. It has been known for a long time that the temperature coefficient of velocity of the nerve impulse is greater than that of most purely physical processes. We find that the temperature coefficient of carbon dioxide production of the non-stimulated nerve is of about the same magnitude as that of the velocity of the nerve impulse.

Basing our conclusions on the foregoing experimental facts, we consider the nature of the nerve impulse as follows:

There are two chemical conditions necessary to enable the nerve to conduct the nerve impulse.

The first condition is the maintenance of normal chemical activity, i.e., the presence of certain chemically unstable substances. Just what these substances are, we do not know. This condition constitutes, to my mind, the so-called state of excitability. The nerve must be in this condition to be capable of response to a stimulus. The instability of these substances enables the nerve to undergo greater chemical changes when stimulated; that is, stimulation is accompanied by an increase in chemical activity. This is true not only for nerve tissue, but also for all other living tissues, including living seeds. The second condition is, if this increase in chemical change at the point of stimulus is sufficiently greater than that in its neighborhood, the impulse will go in that direction. The normal nerve impulse, therefore, will go only in one definite direction. The possibility of nerve conduction in two

* In this connection it is interesting to note that carbon dioxide production from medullated nerves is not always greater than from non-medullated ones, in spite of the fact that medullated nerves invariably carry the nerve impulse much more quickly than non medullated ones. This is rather important in view of the fact that the conducting mass in the medullated fiber is known to be much less than that in the non-medullated, if we compare the total nerve fibers gram for gram. It is very likely that if we could compare the carbon dioxide production from the reacting masses of the two nerve fibers, the relative rate of metabolism of the axis cylinder of the medullated fiber would be greater than that of the non-medullated. Since such a comparison is practically impossible at present, the only way to test the correctness of our hypothesis will be to make a series of carbon dioxide measurements on various medullated fibers and compare them with their corresponding rates of nerve impulse. If this relation proves to be general, then not only our current notion that the function of the medullary sheath is to supply nutrition to the conducting medium will be proved correct, but also we may easily understand the morphological development of the medullary sheath in relation to the functional activity of the nerve fiber.

directions is obvious. It must depend on the gradient of chemical activity along the fiber, and the amount of increase of this activity at the point of stimulation.

I believe the nerve impulse is a propagation of chemical change—the propagation being due to a restoration of an equilibrium disturbed by the increase of metabolism at the point of stimulus. This propagation is always toward the point where there is less chemical activity, as measured by carbon dioxide production.

[1] *Amer. J. Physiol.*, 35, 340.

A POINT SCALE FOR MEASURING MENTAL ABILITY

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Alfred Binet, in 1905, devised a method of roughly estimating the intellectual capacity, or degree of mental development, of the child in terms of age. The method depended upon the application of series of single tests or measures, each series being especially arranged for a particular year of age. If a subject could satisfactorily meet the requirements for his age, he was considered up to the standard. Obviously he might measure either a certain number of years above or below the expected intellectual age.

The Binet measuring scale of intelligence has been revised, perfected, and adapted by various individuals, and now after nearly ten years of practical application, it stands as the only convenient and reasonably expeditious method of classifying children with respect to intelligence. It possesses, however, many serious defects which may not now be enumerated, since the purpose of this abstract is to present a brief description of a new method which is based, on the one hand upon the work of Binet and his associates, and on the other upon a suggestion made by the late E. B. Huey. We may call this new method the point scale for measuring mental capacity. It has been developed at the Psychopathic Hospital, Boston, as one result of the demand for reasonably detailed and reliable information concerning the mental characteristics of individuals both immature and mature. The scale consists of a single series of measurements to be made on all subjects. Each measurement is evaluated according to a graded scale, and the maximum credit obtainable in an examination is one hundred points. The